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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,116	08/18/2006	Hideaki Umeyama	079088-0102	2809

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FOLEY AND LARDNER LLP  
SUITE 500  
3000 K STREET NW  
WASHINGTON, DC 20007

EXAMINER
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CLOW, LORI A

ART UNIT	PAPER NUMBER
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1631

MAIL DATE	DELIVERY MODE
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07/13/2010

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/590,116	<b>Applicant(s)</b> UMEYAMA ET AL.	
	<b>Examiner</b> LORI A. CLOW	<b>Art Unit</b> 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 26 April 2010.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-31 is/are pending in the application.
- 4a) Of the above claim(s) 8,9,18,19,28 and 29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7,10-17,20-27,30 and 31 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 18 August 2006 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>8/18/2006; 3/3/2010</u> .                                     | 6) <input type="checkbox"/> Other: _____                          |

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## **DETAILED ACTION**

### **Election/Restrictions**

Applicant's election of Species B, claims 10, 20, and 30 in the reply filed on 26 April 2010 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 8, 9, 18, 19, 28, and 29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 26 April 2010.

Claims 1-7, 10-17, 20-27, 30, and 31 are under exam herein.

### **Priority**

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. This Application claims foreign priority to JP 2004-048767, filed 24 February 2004.

### **Information Disclosure Statement**

The Information Disclosure Statements filed 18 August 2006 and 3 March 2010 have been considered. Signed copies of PTO Forms 1449 are included with this Office Action.

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**Drawings**

The Drawings submitted 18 August 2006 are not accepted. This application contains sequences in Figure 22, 29, and 36 with no associated SEQ ID NOs. Therefore this application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). Applicants are also reminded that SEQ ID Nos are not required in Figures per se, however, the corresponding SEQ ID Nos then are required in the Brief Description of the Drawings section in the specification. Applicants are also reminded that a CD-ROM sequence listing submission may replace the paper and computer readable form sequence listing copies. Applicant(s) are given the same response time regarding this failure to comply as that set forth to respond to this office action. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this Office action.

**Sequence Compliance**

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR § 1.821 through 1.825 because sequences with no corresponding sequence identification numbers appear in Figures 22, 29, and 36 and also at page 112. No sequence listing has been filed. Applicants are given the same response time regarding this failure to comply as that set forth to respond to this office action. A complete response to this office action includes compliance with this sequence rule compliance requirement. Failure to comply may result in abandonment of this application.

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**Specification**

35 U.S.C. 112, first paragraph, requires the specification to be written in "full, clear, concise, and exact terms." The specification is replete with terms which are not clear, concise and exact. The specification should be revised carefully in order to comply with 35 U.S.C. 112, first paragraph. The Specification is replete with grammatical errors that are required to be corrected.

**Claim Objections**

Claims 2, 12, and 22 are objected to because of the following informalities: Please correct mistakes in all claims.

Claims 2, 12, and 22 recite, "shown in Formula 1." This is improper claim format and the claim should be amended to read, "shown in Formula 1:"

Claims 2, 12, and 22 contain parentheses after the recitation of Formula 1. This is improper format. Parentheses should be removed.

Claims 2, 12, and 22 are missing a period at the end of the claim. Please correct.

Claims 7, 17, and 27 recites, "shown by Formula 2 and Formula 3." This is improper claim format and the claim should be amended to read, "shown in Formula 2 and Formula 3:"

Claims 7, 17, and 27 contain parentheses after the recitation of Formula 3. This is improper format. Parentheses should be removed.

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**Claim Rejections - 35 USC § 101-Non-statutory Subject Matter**

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 11-17, 20-27, 30, and 31 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 11-17 and 20 are drawn to a method which screens for a ligand that binds to a protein when coordinate data of a protein of a single chain or plural chain is given.

In accord with the decision in *In re Bilski* (cited below), a claim to a process or method must meet the machine-or-transformation test in order to be eligible under 35 USC 101 as statutory subject matter (*In re Bilski*, 545 F.3d 943, 88 USPQ2d 1385 (Federal Circuit, 2008)). In other words, the prohibition on patenting abstract ideas has two distinct aspects: (1) when an abstract concept has no claimed practical application, it is not patentable; (2) while an abstract concept may have a practical application, a claim reciting an algorithm or abstract idea can state statutory subject matter only if it is embodied in, operates on, transforms, or otherwise is tied to another class of statutory subject matter under 35 U.S.C. §101 (i.e. a machine, manufacture, or composition of matter). (*Gottschalk v. Benson*, 409 U.S. 63, 175 USPQ 673, 1972), as clarified in *In re Bilski*, 545 F.3d 943, 88 USPQ2d 1385 (Federal Circuit, 2008) the test for a method claim is whether the claimed method is (1) tied to a particular machine or apparatus or (2) transforms a particular article to a different state or thing.

In the instant case, the method claims are not so tied to another statutory class of invention because the method steps that are critical to the invention are "not tied to any

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**particular apparatus or machine**” nor do the steps provide a transformation of data and therefore do not meet the machine-or-transformation test as set forth in *In re Bilski* 545 F.3d 943, 88 USPQ2d 1385 (Federal Circuit, 2008).

In addition to the above analysis claims 21-27, 30, and 31 recite “a program” and a “computer readable recording medium”. A computer product that is readable by a computing system is drawn to non-statutory subject matter because a computer product reads on a computer-readable medium which reads on carrier waves, which read on transitory propagating signals which are not proper patentable subject matter because they do not fit within any of the four statutory categories of invention (*In re Nuijten*, Federal. Circuit, 2006). The instant Specification is silent with regard to the specific embodiments encompassed by a program or a computer readable medium, therefore the Specification is interpreted to embody both transitory and non-transitory media and the claims are not statutory.

Applicant is referred to the OG Notice of February 23, 2010 for Subject Matter Eligibility of Computer Readable Media:

<http://www.uspto.gov/web/offices/com/sol/og/2010/week08/TOC.htm#ref20>

It is noted that claims 1-7 and 10 are statutory as the claims to an apparatus include sufficient structure.

### **Claim Rejections - 35 USC § 112**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claim 1-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors.

Claims 1-31 contain numerous grammatical errors, such as missing articles “a” and “the”. For example, claim 1 should read as follows:

**a** post-structural-change protein coordinate data selecting unit that effects structural change in consideration of dynamic behavior using **an** induced-fit parameter reflecting an induced fit on the coordinate data of **the** protein and selects post-structural-change protein coordinate data;

**a** spatial point designating unit that designates a spatial point at which superposition with the ligand is to be conducted from **(delete comma here)** the post-structural-change protein coordinate data selected by the post-structural-change protein coordinate data selecting unit;

**an** interaction function calculating unit that calculates an interaction function when the protein and the ligand bind to each other using the spatial point designated by the spatial point designating unit and a ligand coordinate data of the ligand; and

**a** ligand evaluating unit that evaluates the ligand that binds to the protein based on the interaction function calculated by the interaction function calculating unit.

Please correct mistakes in all claims.



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Claims 1, 11, and 21 recite, “post-structural-change protein coordinate data selecting unit that effects structural change in consideration of dynamic behavior”. It is unclear as to what is intended by this limitation. Does the selecting unit make a structural change in the protein based on protein dynamic behavior, for example? Clarification through clearer claim language is requested.

Claims 1, 11, and 21 recite, "spatial point designating unit that designates a spatial point at which superposition with the ligand is to be conducted". It is unclear as to whether this is an active step or an intended step. Perhaps Applicant intends that claim to read, “a spatial point designating unit that designates a spatial point at which superposition with the ligand is conducted from the post-structural-change protein coordinate data”. Clarification through clearer claim language is requested.

Claims 5, 15, and 25 recite, "reevaluating unit that executes the interaction function calculating unit". It is unclear if the reevaluating unit interacts with the calculating unit or if some other function occurs. Please correct claim language.

Claims 7, 17, and 27 recite, “Krot”. It is unclear as to what Krot represents in the formula, as it is not defined by any parameter. Clarification is requested.

Claims 7, 17, and 27 recite, “Kpos”. It is unclear as to what Kpos represents in the formula, as it is not defined by any parameter. Clarification is requested.

### **Claim Rejections - 35 USC § 102**

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

**1. Claims 1, 3-6, 10, 11, 13-16, 20, 21, 23-26, 30, and 31 are rejected under 35**

U.S.C. 102(a) as being anticipated by Hammer et al. (Steroids (2003) Vol. 68, pages 329-339; PTO Form 1449 Reference).

The instant claims are drawn to an apparatus, method and program for ligand screening in which coordinate data and induced fit parameter modeling is used to model protein binding; superposition of a ligand using spatial points is performed; interaction of protein and ligand are calculated' and binding is evaluated.

In regard to the instant claims, Hammer et al. teach a method and system for interactions of glucocorticoids (GC) with ligand-binding domains of the glucocorticoid receptor (GR) using molecular modeling including ligand docking and molecular dynamics simulations (abstract). A ligand binding domain (LBD) was modeled using SURFNET software taking into consideration the free space in the LBD (page 333, column 1). Induced fit procedures were used by molecular dynamics simulation using INSIGHT/DISCOVER software and protein quality was controlled by PROCHECK software that monitored changes (the dynamics) of the binding pocket. Superimposition was employed using 3D QSAR analysis to evaluate the interaction fields

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between the ligand and receptor. Biological activity was assessed using partial least squares (page 333, column 1-2).

2. Claims 1-7, 10-17, 20-27, 30, and 31 are rejected under 35 U.S.C. 102(e) as being anticipated by WO 2002/057954.

The instant claims are drawn to an apparatus, method and program for ligand screening in which coordinate data and induced fit parameter modeling is used to model protein binding; superposition of a ligand using spatial points is performed; interaction of protein and ligand are calculated' and binding is evaluated.

WO 2002/057954 teaches a method and system of induced fit conformation modeling of a protein using atomic coordinate data (Detailed Description; from Raw Machine Translation provided by the Japan Patent Office available at:

[http://dossier1.ipdl.inpit.go.jp/AIPN/odse\\_top\\_dn.ipdl?N0000=7400](http://dossier1.ipdl.inpit.go.jp/AIPN/odse_top_dn.ipdl?N0000=7400))

The document teaches the following with respect to the claims:

“First, in construction of the conformation of object protein, the protein (reference protein) which inputs and refers to the amino acid sequence of object protein is selected. Selection of reference protein is performed using the known alignment software. The atomic coordinate of this reference protein is acquired from a suitable conformation database. An atomic coordinate is optimized using the objective function which comprises an atomic coordinate of reference protein.”

Further, the reference discloses that , “the atomic coordinate is displaced using the optimization coordinate created at the above-mentioned step. As for displacement of an atomic

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coordinate, it is preferred to perform the normal vibration analyzing method and to carry out by obtaining the characteristic vector of each characteristic value. In that case, the coordinate system which makes flexibility a part of optimized flexibility may be used. In this case, optimization is attained also to a part of flexibility”.

In addition, the document teaches interaction function mathematical manipulations and molecular dynamic calculations (see entire document).

**3.** Claims 1, 3-6, 10, 11, 13-16, 20, 21, 23-26, 30, and 31 are rejected under 35 U.S.C. 102(e) as being anticipated by US 2003/0190670 A1 (Bursavich et al.; PTO Form 1449 Reference).

The instant claims are drawn to an apparatus, method and program for ligand screening in which coordinate data and induced fit parameter modeling is used to model protein binding; superposition of a ligand using spatial points is performed; interaction of protein and ligand are calculated’ and binding is evaluated.

Bursavich et al. teach a method and system for generating chemical structures of non-peptide inhibitors of biologically-active receptors by constructing models of a receptor-ligand complex using three-dimensional data of the receptor-ligand complex (abstract). The method uses computer modeling programs to model the receptor conformations based on three-dimensional data which is used to construct a mathematical model of the geometry and chemistry of the binding site (paragraph 0013). The model target conformation can be altered based on binding activity and yields a novel conformational model (paragraph 0014) (interaction of ligand and binding site; dynamic behaviors). Within the mathematical model of the conformation of the

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binding site, the receptor site can be altered by modifying various parameters such as energy, spatial interactions etc... (paragraph 0016). The various computer programs that conduct the method are disclosed at paragraphs 0036 to 0053.

No claims are allowed.

### **Inquiries**

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete

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service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

July 13, 2010

/Lori A. Clow, Ph.D./

Primary Patent Examiner

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